However, as detailed below, amended claims 1 and 9 render Examiner's restriction requirement improper under the PCT Rules governing Unity of Invention. Applicants, believe that the amended claims are clearly distinguishable over the cited reference of Turki et al. Accordingly, the claims now posses the special technical feature required by PCT Rules 13.1 and 13.2. Applicants believe in good faith, that the restriction requirement is hereby traversed, and that the claims should be evaluated on the merits.

Election of Species

1. Amended independent claims 1 and 9 recite base substitutions of $\beta 2$ adrenergic receptor. For the purpose of examination, Applicants elect substitutions, i.e., alleles at positions 1541 and 1568.

2. Examiner further requires election of a single disease. Applicants elect hypertension/high blood pressure.

Applicants assert their option to rejoin non-elected species upon allowance of a generic claim.

The Amended Independent Claims Disclose a Single Inventive Concept

The restriction requirement, as elaborated in items 2 and 3 of the office action (p. 3), are predicated on the: (i) lack of a special technical feature linking Groups I-IV; (ii) claims encompassing a plurality of patentably distinct species of alleles encoding the β2-adrenergic receptor ("β2ar").

"Unity of invention has to be considered in the first place only in relation to the independent claims...and *not the dependent claims*." Administrative Instructions Under the PCT, Annex B, Part 1(c) (Emphasis added). In addition, the PCT Rules indicate that if an independent claim avoids the art, it is irrelevant whether a dependent

claim itself contains a further invention. *Id.* Thus, all claims depending on amended claims 1 and 9 are allowable, and share the same special technical feature.

Applicants respectfully point out that the sequence variants at nucleic acid positions 1633, 1666 and 2078 (attributed to the Turki, *et al*) have been deleted from amended independent claims 1 and 9.

Thus, because the amended claims would overcome an obviousness rejection over Turki et al., the amended claims clearly possess a linking special technical feature.

Accordingly, the restriction requirement should be withdrawn.

The inventions described in the claims all share a single inventive concept. Group I's claims are directed to variants of β2ar that are disclosed as pertaining to disease. Group II's claims are directed to methods of determining an individual's genetic predisposition to disease based on whether or not that individual, i.e., a "proband" in genetic testing parlance, possesses one of Group I's variants.

It is inconceivable that these groups should not be viewed as part of a single inventive concept. Group I's claim are directed to disease related β2ar variants; Group II describes a method to determine these variants as well as identifying new ones. *Both* Group I and Group II have the same utilities. In fact, Group I likely has no other utility. *Both* groups are geared toward determining if a genetic variant of β2ar is correlated with a disease. Further, amended independent claim 9 specifically describes the method by which the variants can be detected.

For very similar reasons, the claims of Group III (using the sequence data to chose proper treatments) and Group IV (predicting responsiveness of a genetic predisposition to a treatment) *also share the identical special technical feature.* \

In view of amended independent claims 1 and 9 avoiding the reference, restricting these dependent claims would violate the PCT's guidelines as set forth above and in Annex B. Accordingly, Applicants respectfully request withdrawal of the restriction requirement as to all groups of claims, i.e., I to IV.

Therefore, amended claims 1 and 9 avoid the reference and thus, possess a special technical features shared by *all* the other claims. Therefore, under PCT Rules 13.1 and 13.2, the present restriction requirement should be withdrawn.

CONDITIONAL PETITION FOR EXTENSION OF TIME

If any extension of time for this response is required, Applicants request that this be considered a petition therefore. Please charge the required fee to Deposit Account No. 14-1263.

ADDITIONAL FEES

Please charge any further insufficiency of fees, or credit any excess to Deposit Account No. 14-1263.

CONCLUSION

Applicants have amended independent claims 1 and 9 so as to avoid the Turki reference. These claims, and all dependent therefrom, now share a patentable special technical feature.

Withdrawal of the restriction requirement is respectfully solicited.

Respectfully submitted,

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MARK UP OF AMENDED CLAIMS

1. (Amended) Sequence of the human beta2-adrenergic receptor gene wherein the sequence comprising base substitutions at one or more positions selected from the group consisting of ~~bases have been substituted completely or partly in the~~ positions 159, 245, 565, 934, 1120, 1221, 1541, 1568, ~~1633~~, ~~1666~~, 1839, ~~2078~~, 2110, 2640 and 2826.

9. (Amended) A method for determining dispositions to diseases wherein the DNA of a proband is extracted and analyzed for sequence variations, ~~genotypified at least in one of the substituted positions~~ and ~~subsequently~~ compared with at least one ~~the~~ similarly analyzed reference DNA sequence, ~~if necessary, with all potential combinations of variants from the individual mutation to all potential combinations of all variants being included, including any absolute number of variants~~ wherein the reference DNA sequence comprises a base substitution at one or more positions selected from the group consisting of positions 159, 245, 565, 934, 1120, 1221, 1541, 1568, 1839, 2110, 2640 and 2826, and wherein the method comprises the steps of:

hybridizing at least one pair of primers to genomic DNA comprising the beta2-adrenergic receptor gene under conditions suitable for performing PCR;

amplifying one or more genomic sequences by PCR; and

sequencing the amplified sequences,

analyzing the amplified sequences to discern differences between the proband and reference DNAs.